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FACSIMILE TRANSMISSION SHEET

TO	Examiner Ali Reza Salimi
COMPANY	United States Patent and Trademark Office
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FROM:	Thomas J. Wrona Marshall, Gerstein & Borun	**EXTENSION:**	825
PAGES (INCLUDING THIS PAGE):	5	**CLIENT NO:**	27373
GROUP ART UNIT:	1648	**MATTER NO:**	37922
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MESSAGE: Attached please find a copy of a Response to Restriction Requirement which was filed with the United States Patent and Trademark Office on January 21, 2003 via First Class Mail. Please confirm receipt of this document via facsimile. Thank you.

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#6 Election 1/31/03

Atty Docket No. 27373/37922

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Schwartz *et al.*

Serial No. 09/995,475

Filed: November 28, 2001

Title: Genetically Engineered Herpes Virus For The Treatment of Cardiovascular Disease

Group Art Unit: 1648

Examiner: Ali Reza Salimi

Certificate of First Class Mailing

I hereby certify that this paper is being filed by First Class Mail in an envelope, postage prepaid, addressed to the Commissioner for Patents, Washington, DC 20231.

January 21, 2003

Thomas J. Wrona, Ph.D.

RESPONSE TO RESTRICTION REQUIREMENT

Commissioner For Patents
Washington, DC 20231

Dear Sir:

This paper is filed in response to the office action imposing a restriction requirement that was mailed December 18, 2002 (hereinafter, the "office action"), restricting the claims of the application. This response is timely filed because January 18, 2003 fell on a Saturday and today is the next official business day (Monday, January 20, 2003, was a federal holiday).

The Restriction Requirement set forth a seven-way restriction requirement as follows:

Group I: Claims 1-3, 6-14, drawn to a method of utilizing a herpesvirus expression vector wherein the vector is debilitated by non-silent insertion, substitution or deletion;

Group II: Claims 1, 4-14, drawn to a method of utilizing a herpesvirus expression vector wherein the vector is lacking $\gamma_1 34.5$;

Group III: Claims 1 and 15, drawn to a method of treating herpesvirus infection;

Group IV: Claims 16-18 and 21-29, drawn to a method of treating or preventing cardiovascular disease wherein the vector is debilitated by non-silent insertion, substitution or deletion;

Group V: Claims 16 and 19-29, drawn to a method of treating or preventing cardiovascular disease wherein the vector is lacking $\gamma_1 34.5$;

Group VI: Claims 16 and 30, drawn to a method of treating or preventing cardiovascular and herpes simplex virus infection; and

Group VII: Claims 31-33, drawn to a method of inducing normal physiology.

Applicant provisionally elects the invention of Group II, *i.e.*, claims 1 and 4-14, with traverse.

II. Remarks

The Examiner imposed a seven-way restriction requirement in the Office Action, providing the following reasons in support:

> Inventions of Groups I-VII are directed to mutually exclusive and patentably distinct methods which are functionally and substantially different. The examination of all groups would require different searches in the U.S. Patent Shoes, in house and commercial databases, and scientific literature and would require the consideration of different patentability issues.

The above-quoted two sentences constitute all of the Examiner's reasoning in support of the conclusion that the "inventions" as defined in the office action are distinct. Applicant understands that under current Patent Office practice, a conclusion that inventions are distinct is effectively a conclusion that the inventions are "independent and distinct." *See* M.P.E.P. § 802.01. In response, Applicant respectfully traverses.

The initial burden of establishing a *prima facie* case for restriction is placed on the Patent Office, which must identify the groups of claims and "provide the particular reasons . . . for holding that the inventions as claimed are either independent or distinct . . . . A mere statement of conclusion is inadequate." M.P.E.P. § 816. Applicant respectfully submits that the Examiner has not satisfied his burden. The language quoted above does not provide reasoning in support of the Examiner's

position; rather, the Examiner made two conclusory statements. First, that the methods of the various Groups are mutually exclusive and patentably distinct. Second, that examination of the Groups would require different searches and involve consideration of different patentability issues. The characterization of the methods of the Claim Groups as being "mutually exclusive" cannot be reconciled with the contents of those Groups. For example, claim 1 is identified as a member of Groups I, II, and III; claims 6-14 are members of both Groups I and II; and claim 16 is a member of Groups IV, V, and VI. Because the same claim(s) is found in more than one group, these groups cannot be "mutually exclusive." The Examiner did not supply any other reasons in support of the restriction requirement. Thus, Applicant submits that the Patent Office has not established a *prima facie* case of independent and distinct inventions being claimed. The Patent Office failed to supply any reasons in support of a conclusion that the claims of the various Groups are drawn to distinct inventions, as required by M.P.E.P. § 816. Accordingly, Applicant respectfully submits that the restriction requirement may properly be withdrawn and all of the pending claims may properly be examined in the present application.

Beyond the preceding position, Applicant traverses the exclusion of claims 2 and 15 from Group II. Claim 2 is dependent on claim 1 and is directed to embodiments wherein the herpes simplex virus is debilitated by non-silent insertion, substitution, or deletion of a nucleotide sequence in at least one **non-essential** gene of the herpes simplex virus. As described in the specification, $\gamma_1$34.5 is a non-essential gene (*see, e.g.*, page 5, lines 18-20; Table 3). It would not create an undue burden on the Examiner to search herpes simplex virus debilitated by alteration of a nucleotide sequence in at least one non-essential gene, because this subject matter would be included within the search of claims 1 and 4. Inclusion of claim 2 into Group II is respectfully requested.

The Examiner also requested a species election between non-silent insertion, substitution, or deletion. In support, the Examiner asserted that each species confers different structure and "presumably" different effects on expression vectors. If claim 2 is included in Group II, Applicant provisionally elects "deletion" with traverse. Applicant traverses the restriction between the species because the species, though structurally different, contain functional similarities. Moreover, the Examiner relies on a presumption of different functional effects that is not available under the law nor in agreement with scientific principles. A non-silent insertion, substitution or deletion

of a nucleotide sequence that debilitates a herpes simplex virus, as recited in the claims (*see, e.g.*, claim 2), has the same functional effect, i.e., to debilitate the virus. Speculation, without more, on the possible differing effects of the various modifications on an expression vector is unwarranted under the law or on the present facts. Accordingly, examination of all three species is respectfully requested.

Also, Applicant requests inclusion of claim 15 into Group II. The Restriction inappropriately finds claim 15 drawn to a method of treating herpesvirus infection. Applicant respectfully disagrees. Claim 15 is dependent on claim 1 and is drawn to a method of expressing a heterologous nucleic acid sequence in a vascular cell comprising administering to the cell a recombinant replicating herpes simplex viral vector comprising (1) a heterologous nucleic acid, wherein the herpes simplex virus is debilitated for growth in the central nervous system and (2) at least one gene essential for treatment of a herpes simplex virus infection by an anti-viral agent. The term "essential for the treatment of herpes simplex virus infection by an anti-viral agent" describes the gene, not the purpose of the method. As described in the specification, certain genes, such as thymidine kinase, are essential for the treatment of herpes simplex virus infection by the anti-viral agent acyclovir (*see, e.g.*, example 9). However, claim 15 does not require a step of administering an anti-viral agent. Thus, claim 15 is not directed to different subject matter than claim 1; rather, claim 15 merely further limits the herpes simplex virus that is administered. Inclusion of claim 15 in Group II is respectfully requested.

Applicant reserves the right to pursue claims directed to the subject matter of any canceled claims in duly filed continuing applications.

Respectfully submitted,

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January 20, 2003

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